ethylcysteine, S-benzylcysteine, homoserine, 4-dehydroproline, penicillamine β-(2-thienyl)alanine, NH_2-CH(CH_2CHEt_2)-COOH, α-aminoheptanoic acid, NH_2-CH(CH_2-1-naphthyl)-COOH, NH_2-CH(CH_2-2-naphthyl)-COOH, NH_2-CH(CH_2-cyclohexyl)-COOH, NH_2-CH[CH-(cyclohexyl)$_2$]-COOH, NH_2-CH(CH_2-cyclopentyl)-COOH, NH_2-CH[CH-(cyclopentyl)$_2$]-COOH, NH_2-CH(CH_2-cyclobutyl)-COOH, NH_2-CH[CH-(cyclobutyl)$_2$]-COOH, NH_2-CH(CH_2-cyclopropyl-COOH, NH_2-CH[CH-(cyclopropyl)$_2$]-COOH, 5,5,5-trifluoroleucine, hexafluoroleucine, (S)-azetidine-2-carboxylic acid, (S)-pipecolic acid, (S)-oxazolidine-4-carboxylacid (L-thioproline), sarcosine;

f) residue selected from the group consisting of 3-aminobenzoic acid; ε-aminocaproic acid, β-alanine;

g) Y-NH-CO-NH-;

h) Y'O_2CCH(NHCO-Y)CH_2-;

i) Y'NHCO-;

j) CH_3-O-CO-Y'-NH-CO-;

k) CH_3-CH_2-O-CO-Y'-NH-CO-;

l) H, halogen, NO_2, CN, OH, COOH;

m) amino, C_1-C_6 alkylamine, C_2-C_{12} dialkylamino;

n) C_1-C_6 acyl;

o) C_1-C_6 alkoxy-CO-; and

p) C_1-C_6 alkyl-S-,

wherein Y is C_1-C_6 alkyl, aryl or H and Y' is C_1-C_6 alkyl, and pharmaceutically acceptable salts thereof.

2. The compound of claim 1, wherein X is a moiety of the general formula $(AA)_p$-aa-, wherein:

p indicates that there may be 0, 1, 2, 3, 4 or 5 residues AA, which can be the same or different within one molecule;

AA and aa are α-amino carboxylic acids with in α position an optionally substituted C_1-C_6 alkyl or aryl or aralkylmoiety; and

pharmaceutically acceptable salts thereof.

3. The compound of claim 1, wherein X is a moiety of the general formula $(AA)_p$-aa-, wherein:

p indicates that there may be 0, 1, 2, 3, 4 or 5 residues AA, which can be the same or different within one molecule;

AA and aa are selected from the group consisting of: alanine, methionine, methionine sulfoxide, arginine, homoarginine, phenylalanine, aspartic acid, proline, hydroxyproline, asparagine, serine, cysteine, threonine, histidine, glycine, tyrosine, glutamic acid, pyroglutamic acid, trytophan, glutamine, valine, norvaline, isoleucine, lysine, leucine, norleucine, thioproline, homoproline, 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (Tic), 2,3-dihydroindol-2-carboxylic acid, α-naphtylglycine, α-phenylglycine, 4-amidinophenylglycine, 4-phenylproline, 4-amidinophenylalanine, O-benzyl tyrosine, omega-acetyl lysine, α-aminobutyric acid, citrulline, homocitrulline, ornithine, O-methylserine, O-ethylserine, S-methylcysteine, S-ethylcysteine, S-benzylcysteine, homoserine, 4-dehydroproline, penicillamine β-(2-thienyl)alanine, NH_2-CH(CH_2CHEt_2)-COOH, α-aminoheptanoic acid, NH_2-CH(CH_2-1-naphthyl)-COOH, NH_2-CH(CH_2-2-naphthyl)-COOH, NH_2-CH(CH_2-cyclohexyl)-COOH, NH_2-CH[CH-(cyclohexyl)$_2$]-COOH, NH_2-CH(CH_2-cyclopentyl)-COOH, NH_2-CH[CH-(cyclopentyl)$_2$]-COOH, NH_2-CH(CH_2-cyclobutyl)-COOH, NH_2-CH[CH-(cyclobutyl)$_2$]-COOH, NH_2-CH(CH_2-cyclopropyl)-COOH, NH_2-CH[CH-(cyclopropyl)$_2$]-COOH, 5,5,5-trifluoroleucine, hexafluoroleucine, (S)-azetidine-2-carboxylic acid, (S)-pipecolic acid, (S)-oxazolidine-4-carboxylic acid, (R)-thiazolidine-4-carboxylacid (L-thioproline), 3-aminobenzoic acid, sarcosine, ε-aminocaproic acid, β-alanine, wherein the alpha amino residue may be side chain blocked or unblocked and has the L, D, or DL configuration at the alpha carbon atom; and

pharmaceutically acceptable salts thereof.

4. The compound of claim 2, wherein AA is lysine or ornithine, and the amino side chain thereof is involved in an intramolecular covalent bond.

5. The compound of claim 2, wherein X is M-$(AA)_p$-aa-, wherein:

M is selected from:

a) the group consisting of optionally substituted -$CONH_2$, -$CSNH_2$, -SO_2NH_2, phenyl-SO_2-, phenyl-CH_2SO_2-, 2-furyl-acryloyl;

b) the group of protecting group consisting of: acetyl, adamantyloxycarbonyl, benzyloxycarbonyl, benzoyl, benzyl, t-butoxycarbonyl, t-butyl, 2,4-dinitrophenyl, formyl, fluorenylmethoxycarbonyl, 4-methoxybenzyl, tosyl, trifluoroacetyl, trityl, phthaloyl, phenylalkylcarbonyl, 2-indanylacetyl, 2-(1,2,3,4-tetrahydronaphtyl)acetyl, 4-(4-benzylphenoxy) alkyl; and

pharmaceutically acceptable salts thereof.

6. The compound of claim 2, wherein X represents (M-)AA-aa-, M may or may not be present and aa is proline.

7. The compound of claim 2, wherein X represents (M-)AA-aa-, wherein M may or may not be present, and wherein AA and aa are both proline.

8. The compound of claim 2, wherein aa is alanine and R1 and R2 are selected from the group consisting of:

l) H, halogen, NO_2, CN, OH, COOH;

m) amino, C_1-C_6 alkylamine, C_2-C_{12} dialkylamino;

n) C_1-C_6 acyl;

o) C_1-C_6 alkoxy-CO-;

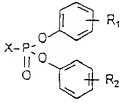
p) C_1-C_6 alkyl-S-; and

pharmaceutically acceptable salts thereof.

9. The compound of claim 2, wherein at least the AA coupled to the aa is proline or phenylalanine and pharmaceutically acceptable salts thereof.

10. The compound of claim 9, which compound is Phe-Ala-diphenylphosphonate or Pro-Ala-diphenylphosphonate and pharmaceutically acceptble salts thereof.

11. The compound of claim 1, having the general formula:



(II)

and pharmaceutically acceptable salts thereof.

12. The compound of claim 11, selected from the group consisting of:

Di(3-acetamidophenyl) 1-(benzyloxycarbonyl-(S)-prolyl)pyrrolidine-2(R,S)-phosphonate;

Di(4-acetamidophenyl) 1-(benzyloxycarbonyl-(S)-prolyl)pyrrolidine-2(R,S)-phosphonate;

Di(4-methylsulfonylaminophenyl) 1-(benzyloxycarbonyl-(S)-prolyl)pyrrolidine-2(R,S)-phosphonate;

Di(3-ureylphenyl) 1-(benzyloxycarbonyl-(S)-prolyl)pyrrolidine-2(R,S)-phosphonate;

Di[4-(N-benzoylglycylamino)phenyl]-1-(benzyl-oxycarbonyl-(S)-prolyl)pyrrolidine-2(R,S)-phosphonate;

Di[4-(N-glycylamino)phenyl]-1-(benzyloxycarbonyl-(S)-prolyl)pyrrolidine-2(R,S)-phosphonate;

Di[4-(N-benzyloxycarbonyl-(S)-alanylamino)phenyl]-1-(benzyloxycarbonyl-(S)-prolyl)pyrrolidine-2(R,S)-phosphonate;

Di[4-((S)-pyroglutamylamino)phenyl]-1-(benzyloxycarbonyl-(S)-prolyl)pyrrolidine-2(R,S)-phosphonate;

Di{4-[-(S)-(2-methoxycarbonyl-2-acetamido)ethyl]-phenyl}1-(benzyloxycarbonyl-(S)-prolyl)pyrrolidine-2(R,S)-phosphonate;

Di(4-methoxycarbonylphenyl)1-(tert-butyloxycarbonyl-(S)-prolyl)pyrrolidine-2(R,S)-phosphonate;

Di{4-[(ethoxycarbonyl)methylaminocarbonyl]phenyl} 1-(benzyloxycarbonyl-(S)-prolyl)-pyrrolidine-2(R,S)-phosphonate;

Di{4-[2-(methoxycarbonyl)ethylaminocarbonyl]phenyl}1-(benzyloxycarbonyl-(S)-prolyl)-pyrrolidine-2(R,S)-phosphonate;

Di[4-(n-propylaminocarbonyl)phenyl] 1-(benzyloxycarbonyl-(S)prolyl)-pyrrolidine-2(R,S)-phosphonate;

Di(3-acetamidophenyl) 1-((S)-prolyl)pyrrolidine-2(R,S)-phosphonate hydrochloride;

Di(4-acetamidophenyl) 1-((S)-prolyl)pyrrolidine-2(R,S)-phosphonate hydrochloride;

Di(4-methylsulfonylaminophenyl) 1-((S)-prolyl)-pyrrolidine-2(R,S)-phosphonate hydrochloride;

Di(3-ureylphenyl) 1-((S)-prolyl)pyrrolidine-2(R,S)-phosphonate hydrochloride;

Di[4-(N-benzoylglycylamino)phenyl]-1-((S)-prolyl)-pyrrolidine-2(R,S)-phosphonate hydrochloride;

Di[4-(N-glycylamino)phenyl]-1-((S)-prolyl)-pyrrolidine-2 (R,S)-phosphonate trihydrochloride;

Di(4-(S)-alanylaminophenyl)-1-((S)-prolyl)pyrrolidine-2(R,S)-phosphonate trihydrochloride;

Di(4-(S)-pyroglutamylaminophenyl)-1-((S)-prolyl)-pyrrolidine-2(R,S)-phosphonate hydrochloride;

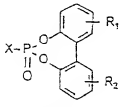
Di{4-[-(S)-(2-methoxycarbonyl-2-acetamido)ethyl]-phenyl} 1-((S)-prolyl)-pyrrolidine-2-phosphonate hydrochloride; Di{4-[(ethoxycarbonyl)methylaminocarbonyl]phenyl} 1-((S)-prolyl)pyrrolidine-2(R,S)-phosphonate;

Di{4-[2-(methoxycarbonyl)ethylaminocarbonyl]phenyl} 1-((S)-prolyl)-pyrrolidine-2(R,S)-phosphonate hydrochloride;

Di[4-(n-propylaminocarbonyl)] 1-((S)-prolyl)-pyrrolidine-2(R,S)-phosphonate hydrochloride; and

pharmaceutically acceptable salts thereof.

13. The compound of claim 1, wherein the compounds are 2,2' biphenyl diesters of α-aminoalkyl phosphonic acid having the general formula:



(III)

and pharmaceutically acceptable salts thereof.

14. The compound of claim 13, selected from the group consisting of:

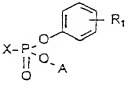
2,2'-Biphenyl 1-(benzyloxycarbonyl-(S)-prolyl)-pyrrolidine-2(R,S)-phosphonate;

2,2'-Biphenyl 1-(t-butyloxycarbonyl-(S)-prolyl)-pyrrolidine-2(R,S)-phosphonate; and

2,2'-Biphenyl 1-((S)-prolyl)pyrrolidine-2(R,S)-phosphonate hydrochloride.

15. The compound of claim 14, which compound is 2,2'-Biphenyl 1-((S)-prolyl)pyrrolidine-2(R,S)-phosphonate hydrochloride or a pharmaceutically acceptable salt thereof.

16. The compound of claim 2, having the general formula:



(IV)

wherein A is H, C_1-C_6 alkyl or halogenoalkyl, except perfluoroalkyl, or pharmaceutically acceptable salts thereof.

17. The compound of claim 16, which compound is 2-(2'-Hydroxyphenyl)phenyl methyl 1-(S)-prolyl)-pyrrolidine-2(R,S)-phosphonate hydrochloride.

18. The compound of claim 1, wherein R1 and/or R2 is selected from the group consisting of 3-AcNH, 4-AcNH, 4-$MeSO_2NH$, 4-(N-Bz-Gly-NH), 4-(H-(S)-Ala-NH, 4-[(2S)-$MeO_2CCH(NHAc)CH_2$], 4-(S)-Pyr-NH, 4-(EtO_2CCH_2NHCO), 4-[$MeO_2C(CH_2)_2NHCO$], 4-[$CH_3(CH_2)_2NHCO$].

19. The compound of claim 5, wherein R1 and/or R2 is selected from the group consisting of 3-AcNH, 4-AcNH, 4-$MeSO_2NH$, 4-(N-Bz-Gly-NH), 4-(H-(S)-Ala-NH, 4-[(2S)-$MeO_2CCH(NHAc)CH_2$], 4-(S)-Pyr-NH, 4-(EtO_2CCH_2NHCO), 4-[$MeO_2C(CH_2)_2NHCO$], 4-[$CH_3(CH_2)_2NHCO$].

20. A pharmaceutical preparation comprising one or more of the compounds claimed in claim 1 and a suitable excipient, carrier or diluent.

21. The pharmaceutical preparation of claim 20, further comprising one or more additional therapeutic ingredients.

22. A method for *in vitro* modulating protease activity comrpising the step of adding to a solution containing a peptide a concentration of the compound of claim 1 effective to modulate protease activity in the solution.

23. The method of claim 22, wherein the protease activity results in the unwanted degradation of a peptide substrate prior to measurement of the peptide substrate in a peptide assay.

24. A method for *ex vivo* inhibiting protease activity comprising the step of adding to a medium containing cells or organs a concentration of the compound of claim 1 effective to modulate protease activity in the medium.

25. The method of claim 24, wherein the cells or organs are for transplantation.

26. A method for *in vivo* modulating protease activity comprising the step of administering to a living organism an amount of the compound of claim 1 effective to modulate serum protease activity in the organism.